

CLAIMS

What is claimed is:

1. An isolated nucleic acid encoding a fibroblast growth factor-1
5 resistant to thrombin degradation, wherein said nucleic acid comprises the sequence of SEQ ID NO:3.
2. An isolated nucleic acid encoding a fibroblast growth factor-1
resistant to thrombin degradation, wherein said nucleic acid comprises the sequence of
10 SEQ ID NO:1 and further wherein the triplet set of nucleotides CGG at position number 443 to 445 in SEQ ID NO:1 is substituted with a triplet set of nucleotides selected from the group consisting of AAA and AAG.
3. An isolated nucleic acid encoding a fibroblast growth factor-1
15 resistant to thrombin degradation, wherein said nucleic acid comprises the sequence of SEQ ID NO:1 and further wherein the triplet set of nucleotides CGG at position number 443 to 445 in SEQ ID NO:1 is substituted with the triple set of nucleotides AAA.
4. An isolated nucleic acid encoding a fibroblast growth factor-1
20 resistant to thrombin degradation, wherein said nucleic acid comprises the sequence of SEQ ID NO:1 and further wherein the triplet set of nucleotides at position number 443 to 445 in SEQ ID NO:1 is not CGG, CGT, CGC, CGA, AGA, or AGG.
5. An isolated nucleic acid encoding a fibroblast growth factor-1
25 resistant to thrombin degradation, wherein said nucleic acid consists of the sequence of SEQ ID NO:3.
6. An isolated nucleic acid encoding a fibroblast growth factor-1
30 resistant to thrombin degradation, wherein said nucleic acid encodes a polypeptide

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- comprising the amino acid sequence of SEQ ID NO:4.
7. An isolated nucleic acid encoding a fibroblast growth factor-1
resistant to thrombin degradation, wherein said nucleic acid encodes a polypeptide
5 wherein the amino acid residue at position number 136 in SEQ ID NO:2 is lysine.
8. An isolated nucleic acid encoding a fibroblast growth factor-1
resistant to thrombin degradation, wherein said nucleic acid encodes a polypeptide
wherein the amino acid residue at position number 136 of SEQ ID NO:2 is not
10 arginine.
9. An isolated nucleic acid encoding a fibroblast growth factor-1
resistant to thrombin degradation, wherein said nucleic acid encodes a polypeptide
consisting of the amino acid sequence of SEQ ID NO:4.
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10. The isolated nucleic acid of claim 1, wherein said nucleic acid
comprises a nucleic acid specifying a promoter/regulatory sequence operably linked
thereto.
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11. A vector comprising the isolated nucleic acid of claim 1.
12. The vector of claim 11, said vector further comprising a nucleic
acid specifying a promoter/regulatory sequence operably linked thereto.
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13. A recombinant cell comprising the vector of claim 11.
14. A recombinant cell comprising the vector of claim 12.
15. The recombinant cell of claim 13, wherein said cell is selected from
30 a prokaryotic cell, and a eukaryotic cell.

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16. A recombinant cell comprising the isolated nucleic acid of claim 1.

17. The recombinant cell of claim 15, wherein said recombinant cell is
5 a mammalian cell.

18. A transgenic non-human mammal comprising the isolated nucleic
acid of claim 1.

10 19. A transgenic non-human mammal comprising the isolated nucleic
acid of claim 5.

15 20. An isolated polypeptide encoded by an isolated nucleic acid
encoding a fibroblast growth factor-1 resistant to thrombin degradation, wherein said
nucleic acid comprises the sequence of SEQ ID NO:3, or a fragment or derivative
thereof.

21. An isolated fibroblast growth factor-1 polypeptide comprising the
amino acid sequence of SEQ ID NO:4, or a fragment or derivative thereof.

20 22. The isolated fibroblast growth factor-1 polypeptide of claim 21,
said polypeptide comprising from about amino acid 14 to amino acid residue 154
relative to SEQ ID NO:4.

25 23. The isolated fibroblast growth factor-1 polypeptide of claim 21,
said polypeptide comprising from about amino acid 15 to amino acid residue 154
relative to SEQ ID NO:4.

30 24. The isolated fibroblast growth factor-1 polypeptide of claim 21,
wherein said polypeptide is resistant to thrombin degradation, and further wherein said

polypeptide does not comprise an arginine amino acid residue at amino acid number 136 relative to SEQ ID NO:4.

25. The isolated fibroblast growth factor-1 polypeptide of claim 21,
5 wherein said polypeptide is resistant to thrombin degradation, and further wherein said polypeptide comprises a lysine amino acid residue at amino acid number 136 relative to SEQ ID NO:4.

26. An isolated fibroblast growth factor-1 polypeptide consisting of the
10 amino acid sequence of SEQ ID NO:4.

27. A composition comprising an isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin degradation, wherein the nucleic acid comprises the sequence of SEQ ID NO:3, or fragment, or derivative thereof, and a
15 pharmaceutically acceptable carrier.

28. A composition comprising an isolated fibroblast growth factor-1 polypeptide comprising the amino acid sequence of SEQ ID NO:4, or fragment, or derivative thereof, and a pharmaceutically acceptable carrier.
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29. An antibody that specifically binds with a fibroblast growth factor-1 polypeptide comprising the amino acid sequence of SEQ ID NO:4, or fragment, or derivative thereof.

30. The antibody of claim 29, wherein said antibody is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, a humanized antibody, a chimeric antibody, and a synthetic antibody.
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31. An antibody that specifically binds with a polypeptide encoded by
30 an isolated nucleic acid encoding a fibroblast growth factor-1 resistant to thrombin

degradation, wherein said nucleic acid comprises the sequence of SEQ ID NO:3, or a fragment or derivative thereof.

32. A composition comprising an antibody that specifically binds with
5 an isolated mutant fibroblast growth factor-1 polypeptide comprising the amino acid sequence of SEQ ID NO:4, or a fragment or derivative thereof, and a pharmaceutically-acceptable carrier.

33. A method of treating a disease or disorder responsive to
10 administration of fibroblast growth factor 1 (FGF-1) in a mammal, said method comprising administering to said mammal an effective amount of a FGF-1 resistant to thrombin degradation, or a fragment or derivative thereof, thereby treating a disease or disorder responsive to administration of FGF-1 in a mammal.

15 34. The method of claim 33, wherein said degradation resistant FGF-1 is FGF-1_{R136K}.

20 35. The method of claim 34, wherein the amino acid sequence of said FGF-1_{R136K} consists of SEQ ID NO:4.

36. The method of claim 33, wherein said disease or disorder is selected from the group consisting of myocardial ischemia, peripheral vascular disease, cerebral ischemia, epithelial injury, epidermal wound injury, nerve injury, and bone damage.

25 37. A method of enhancing the effectiveness of an FGF-1 response in a mammal wherein the activity of wild-type FGF-1 degraded by thrombin, said method comprising administering to said mammal an effective amount of a thrombin-degradation resistant FGF-1, or a fragment or derivative thereof, thereby enhancing said FGF-1 response in a mammal.

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38. The method of claim 37, wherein said FGF-1 response is selected from the group consisting of a vascular response, a neural response, a regeneration response, a wound healing response, and an endocrine response.

5 39. The method of claim 37, wherein said thrombin degradation resistant FGF-1 is FGF-1_{R136K}.

10 40. A method of stimulating an FGF-1 response in a mammal, wherein said response is inhibited by thrombin degradation of FGF-1, said method comprising administering an effective dose of a thrombin degradation resistant FGF-1, or a fragment or derivative thereof, to said mammal, thereby stimulating an FGF-1 response in a mammal, wherein said response is otherwise inhibited by thrombin degradation of FGF-1.

15 41. The method of claim 40, wherein said thrombin degradation resistant FGF-1 is FGF-1_{R136K}.

20 42. A kit for treating a disease or disorder responsive to administration of FGF-1 in a mammal, said kit comprising an effective amount of a thrombin degradation resistant FGF-1, or a fragment or derivative thereof, said kit further comprising an applicator, and an instructional material for the use thereof.

25 43. The kit of claim 42, wherein said disease or disorder is selected from the group consisting of myocardial ischemia, peripheral vascular disease, cerebral ischemia, epithelial injury, epidermal wound injury, nerve injury, and bone damage.

44. The kit of claim 42, wherein said thrombin degradation resistant FGF-1 is FGF-1_{R136K}.

30 45. A kit for enhancing the effectiveness of an FGF-1 response in a

mammal wherein the activity of wild-type FGF-1 is degraded by thrombin, said kit comprising an effective amount of a thrombin degradation resistant FGF-1, or a fragment or derivative thereof, said kit further comprising an applicator, and an instructional material for the use thereof.

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46. The kit of claim 45, wherein said thrombin degradation resistant FGF-1 is FGF-1_{R136K}.

47. A kit for stimulating an FGF-1 response in a mammal, wherein said 10 response is inhibited by thrombin degradation of FGF-1, said kit comprising an effective dose of a thrombin degradation resistant FGF-1, or a fragment or derivative thereof, said kit further comprising an applicator, and an instructional material for the use thereof.

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48. The kit of claim 47, wherein said thrombin degradation resistant FGF-1 is FGF-1_{R136K}.

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